Magnetic-Field–Induced DNA Strand Breaks in Brain Cells of the Rat

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In previous research, we found that rats acutely (2 hr) exposed to a 60-Hz sinusoidal magnetic field at intensities of 0.1–0.5 millitesla (mT) showed increases in DNA single- and double-strand breaks in their brain cells. Further research showed that these effects could be blocked by pretreating the rats with the free radical scavengers melatonin and *N-tert*-butyl-α-phenylnitrone, suggesting the involvement of free radicals. In the present study, effects of magnetic field exposure on brain cell DNA in the rat were further investigated. Exposure to a 60-Hz magnetic field at 0.01 mT for 24 hr caused a significant increase in DNA single- and double-strand breaks. Prolonging the exposure to 48 hr caused a larger increase. This indicates that the effect is cumulative. In addition, treatment with Trolox (a vitamin E analog) or 7-nitroindazole (a nitric oxide synthase inhibitor) blocked magnetic-field–induced DNA strand breaks. These data further support a role of free radicals on the effects of magnetic fields. Treatment with the iron chelator deferiprone also blocked the effects of magnetic fields on brain cell DNA, suggesting the involvement of iron. Acute magnetic field exposure increased apoptosis and necrosis of brain cells in the rat. We hypothesize that exposure to a 60-Hz magnetic field initiates an iron-mediated process (e.g., the Fenton reaction) that increases free radical formation in brain cells, leading to DNA strand breaks and cell death. This hypothesis could have an important implication for the possible health effects associated with exposure to extremely low-frequency magnetic fields in the public and occupational environments. *Key words:* **apoptosis, DNA strand breaks, free radicals, iron, magnetic field, necrosis.** *Environ Health Perspect* **112:687–694 (2004). doi:10.1289/ehp.6355 available via *http://dx.doi.org/* [Online 27 January 2004]**

Use of electricity exposes people constantly to low-intensity, extremely low-frequency electromagnetic fields, particularly at the power frequencies of 50 and 60 Hz. In previous research (Lai and Singh 1997a),we found that rats acutely exposed to a 60-Hz sinusoidal magnetic field showed an increase in DNA single- and double-strand breaks in their brain cells as measured by the microgel electrophoresis assay. An increase in DNA single-strand breaks was observed after 2 hr of exposure to the magnetic field at flux density of ≥ 0.1 millitesla (mT), whereas an increase in double-strand breaks was observed at ≥ 0.25 mT. Using the microgel electrophoresis assay, Ahuja et al. (1997, 1999), Phillips et al. (1997), Svedenstal et al. (1999a, 1999b), and Zmyslony et al. (2000) have also reported an increase in DNA strand breaks in cells after magnetic field exposure. In studies by Ahuja et al. (1997, 1999), an increase in DNA single-strand breaks in human lymphocytes was observed after 1 hr of exposure to a 50-Hz magnetic field at 0.2–2 mT, whereas in the study by Phillips et al. (1997), an increase in single-strand breaks was observed in human Molt-4 cells after 24 hr of exposure to a 60-Hz magnetic field at 0.1 mT. Svedenstal et al. observed an increase in DNA double-strand breaks in brain cells of mice after 32 days of exposure to magnetic fields of 7.5 μT (Svedenstal et al. 1999a) and after 14 days of exposure at 0.5 mT (Svedenstal et al. 1999b). Zmyslony et al. (2000) reported an increase in single-strand breaks in rat lymphocytes exposed to a 50-Hz magnetic field at 7 mT in the presence of iron cations. More recently, Ivancsits et al. (2002, 2003a, 2003b) reported an increase in DNA single- and double-strand breaks in human fibroblasts intermittently (5 min on/10 min off) exposed to a 50-Hz magnetic field at 1 mT, whereas continuous exposure produced no significant effect. Because the other studies reporting effects of magnetic fields on DNA were carried out under continuous exposure conditions, the results of Ivancsits et al. (2002, 2003a, 2003b) indicate that the interaction of magnetic fields with DNA is quite complicated and apparently depends on many factors. Furthermore, McNamee et al. (2002) reported no significant effect on DNA strand breaks in cerebellar cells of immature mice exposed continuously to a 60-Hz magnetic field at 1 mT for 2 hr. Miyakoshi et al. (2000) reported that a high-intensity (> 50 mT) 50-Hz magnetic field had no significant effect alone, whereas it potentiated X-ray–induced DNA single-strand breaks in human glioma cells. Thus, effects of magnetic fields on DNA may depend on factors such as the mode of exposure, the type of cells studies, and the intensity and duration of exposure.

In the present study, we further investigated the effect and mechanism of interaction of magnetic field exposure on brain cell DNA in the rat. In a previous experiment (Lai and Singh 1997b), we found that pretreating rats with melatonin and a spin-trap compound (*N-tert*-butyl-α-phenylnitrone) blocked the effect of a 60-Hz magnetic field on DNA. Because melatonin and spin-trap compounds are efficient free-radical scavengers, the data suggest that free radicals play a role in the effect of the magnetic field. In another study (Singh and Lai 1998), we found that acute magnetic field exposure induced the formation of DNA–protein and DNA–DNA cross-links in brain cells of rats, which could be the results of free-radical damage involving iron cations (Altman et al. 1995; Lloyd et al. 1997).

In this study, effects of exposure duration and treatments with the vitamin E analog Trolox (Forrest et al. 1994), the nitric oxide synthase inhibitor 7-nitroindazole (Kalisch et al. 1996; Moore and Bland-Ward 1996), and the iron chelator deferiprone (Fredenburg et al. 1996; Kontoghiorghes 1995) were investigated. In addition, incidences of apoptosis and necrosis in brain cells of rats acutely exposed to a 60-Hz magnetic field were studied.

Materials and Methods

Animals. Male Sprague-Dawley rats (2–3 months old, 250–300 g), purchased from B & K Laboratory (Bellevue, WA), were used in this research. They were housed for at least 24 hr before an experiment in the room in which they would be exposed to magnetic fields. The laboratory was maintained on a 12/12-hr light/dark cycle (light on 0700–1900 hr), at an ambient temperature of 22°C and a relative humidity of 65%. Animals were provided with food and water *ad libitum* in their home cages and during exposure.

In vivo *magnetic field exposure system.* A Helmholtz coil pair system was used to expose rats to a sinusoidal 60-Hz magnetic field. This exposure system has been described in detail previously (Lai et al. 1993). Briefly, a computer program was used to design this Helmholtz coil pair system, which can produce a magnetic field with minimal heating and field variations over the exposure area. Each coil is made of two sets of 40 turns each of #6 wire wound in rectangular loops, with minimum internal dimensions of 0.86 × 0.543 m.

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